Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Advanced reproductive age and fertility.

Bibliographic Source(s)

Reproductive Endocrinology and Infertility Committee, Family Physicians Advisory Committee, Maternal-Fetal Medicine Committee, Executive and Council of the Society of Obstetricians, Liu K, Case A. Advanced reproductive age and fertility. J Obstet Gynaecol Can. 2011 Nov;33(11):1165-75. [95 references] PubMed

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

The quality of evidence (I-III) and classification of recommendations (A-E, L) are defined at the end of the "Major Recommendations" field.

Female Advanced Reproductive Age and Infertility

1. Women in their 20s and 30s should be counselled about the age related risk of infertility when other reproductive health issues, such as sexual health or contraception, are addressed as part of their primary well-woman care. Reproductive-age women should be aware that natural fertility and assisted reproductive technology success (except with egg donation) is significantly lower for women in their late 30s and 40s. (II-2A)
2. Because of the decline in fertility and the increased time to conception that occurs after the age of 35, women >35 years of age should be referred for infertility work-up after 6 months of trying to conceive. (III-B)

Assessment of Ovarian Aging

3. Ovarian reserve testing may be considered for women ≥35 years of age or for women <35 years of age with risk factors for decreased ovarian reserve, such as a single ovary, previous ovarian surgery, poor response to follicle-stimulating hormone, previous exposure to chemotherapy or radiation, or unexplained infertility. (III-B)
4. Ovarian reserve testing prior to assisted reproductive technology treatment may be used for counselling but has a poor predictive value for non-pregnancy and should be used to exclude women from treatment only if levels are significantly abnormal. (II-2A)

Treatment of Age-Related Infertility

5. Pregnancy rates for controlled ovarian hyperstimulation are low for women >40 years of age. Women >40 years should consider in vitro fertilization (IVF) if they do not conceive within 1 to 2 cycles of controlled ovarian hyperstimulation. (II-2B)
6. The only effective treatment for ovarian aging is oocyte donation. A woman with decreased ovarian reserve should be offered oocyte donation as an option, as pregnancy rates associated with this treatment are significantly higher than those associated with controlled ovarian hyperstimulation or in vitro fertilization with a woman's own eggs. (II-2B)

Early Pregnancy and Maternal Complications

7. Women should be informed that the risk of spontaneous pregnancy loss and chromosomal abnormalities increases with age. Women should be counselled about and offered appropriate prenatal screening once pregnancy is established. (II-2A)
8. Pre-conception counselling regarding the risks of pregnancy with advanced maternal age, promotion of optimal health and weight, and screening for concurrent medical conditions such as hypertension and diabetes should be considered for women >age 40. (III-B)

Advanced Paternal Age

9. Advanced paternal age appears to be associated with an increased risk of spontaneous abortion and increased frequency of some autosomal dominant conditions, autism spectrum disorders, and schizophrenia. Men >age 40 and their partners should be counselled about these potential risks when they are seeking pregnancy, although the risks remain small. (II-2C)

Definitions:

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

II-1: Evidence from well-designed controlled trials without randomization

II-2: Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group

II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action.

B. There is fair evidence to recommend the clinical preventive action.

C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making.

D. There is fair evidence to recommend against the clinical preventive action.

E. There is good evidence to recommend against the clinical preventive action.

L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making.

*Adapted from The Evaluation of Evidence criteria described in the report of the Canadian Task Force on Preventive Health Care.

†Adapted from the Classification of Recommendations criteria described in the report of the Canadian Task Force on Preventive Health Care.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Age-related infertility (infertility due to advanced maternal or paternal reproductive age)

Guideline Category

Counseling

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Obstetrics and Gynecology

Intended Users

Advanced Practice Nurses

Health Care Providers

Nurses

Patients

Physician Assistants

Physicians

Guideline Objective(s)

To improve awareness of the natural age-related decline in female and male fertility with respect to natural fertility and assisted reproductive technologies (ART) and provide recommendations for their management, and to review investigations in the assessment of ovarian aging

Target Population

Women and men of advanced reproductive age presenting with infertility

Note: Women experience a decline in natural fertility that begins in the mid-30s. There is also an age-related decline in sperm function and male fertility.

Interventions and Practices Considered

Evaluation/Counselling

1. Counselling women about the risk of age-related infertility as part of well-women care
2. Referral of women >35 years for infertility work-up after 6 months of trying to conceive
3. Ovarian reserve testing, including follicle-stimulating hormone testing
4. Counselling women on risks of pregnancy with advanced maternal age
5. Counselling men and their partners on the risk of spontaneous abortion and increased frequency of some autosomal dominant conditions with advanced paternal age

Treatment/Management

1. Ovarian hyperstimulation
2. In vitro fertilization
3. Oocyte donation

Major Outcomes Considered

- Predictive value of ovarian reserve testing
- Pregnancy rates with natural and assisted fertility

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Published literature was retrieved through searches of PubMed or Medline, CINAHL, and The Cochrane Library in June 2010, using appropriate key words (ovarian aging, ovarian reserve, advanced maternal age, advanced paternal age, ART). Results were restricted to systematic reviews, randomized controlled trials/controlled clinical trials, and observational studies. There were no date or language restrictions. Searches were updated on a regular basis and incorporated into the guideline to December 2010.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence Assessment*

I: Evidence obtained from at least one properly randomized controlled trial

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II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

*Adapted from The Evaluation of Evidence criteria described in the report of the Canadian Task Force on Preventive Health Care.

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care. Recommendations for practice were ranked according to the method described in that report (see the "Rating Scheme for the Strength of the Evidence" and the "Rating Scheme for the Strength of the Recommendations" fields).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations†

A. There is good evidence to recommend the clinical preventive action.

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L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making.

†Adapted from the Classification of Recommendations criteria described in the report of the Canadian Task Force on Preventive Health Care.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

This clinical practice guideline has been prepared by the Reproductive Endocrinology and Infertility Committee, reviewed by the Family Physicians

Advisory Committee and the Maternal-Fetal Medicine Committee, and approved by the Executive and Council of the Society of Obstetricians and Gynaecologists of Canada.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Primary and specialist health care providers and women will be better informed about ovarian aging and the age-related decline in natural fertility and about options for assisted reproductive technology.

Potential Harms

- The risk of spontaneous pregnancy loss and chromosomal abnormalities increases with age.
- Pregnancy in women >40 years of age is associated with a higher risk of obstetrical complications, including operative delivery, gestational diabetes, preeclampsia, intrauterine growth retardation, and low birth weight.
- Testing of follicle-stimulating hormone is associated with a false positive rate of 5%.
- There are increased rates of obstetrical and maternal complications with increasing maternal age, including maternal death, hypertension, prematurity, fetal and neonatal death, and operative delivery.

Qualifying Statements

Qualifying Statements

This document reflects emerging clinical and scientific advances on the date issued, and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed. Local institutions can dictate amendments to these opinions. They should be well documented if modified at the local level. None of these contents may be reproduced in any form without prior written permission of the Society of Obstetricians and Gynaecologists of Canada.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 Nov

Guideline Developer(s)

Society of Obstetricians and Gynaecologists of Canada - Medical Specialty Society

Source(s) of Funding

Society of Obstetricians and Gynaecologists of Canada

Guideline Committee

Reproductive Endocrinology and Infertility Committee

Composition of Group That Authored the Guideline

Principal Authors: Kimberly Liu, MD, Toronto ON; Allison Case, MD, Saskatoon SK

Reproductive Endocrinology and Infertility Committee: Anthony P. Cheung, MD (*Co-Chair*), Vancouver BC; Sony Sierra, MD (*Co-Chair*),

Toronto ON; Saleh AlAsiri, MD, Vancouver BC; Belina Carranza-Mamane, MD, Sherbrooke QC; Allison Case, MD, Saskatoon SK; Cathie Dwyer, RN, Toronto ON; James Graham, MD, Calgary AB; Jon Havelock, MD, Burnaby BC; Robert Hemmings, MD, Montreal QC; Francis Lee, MD, Winnipeg MB; Kimberly Liu, MD, Toronto ON; Ward Murdock, MD, Fredericton NB; Vyta Senikas, MD, Ottawa ON; Tannys D.R. Vause, MD, Ottawa ON; Benjamin Chee-Man Wong, MD, Calgary AB

Financial Disclosures/Conflicts of Interest

Disclosure statements have been received from all members of the committee.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Society of Obstetricians and Gynaecologists of Canada (SOGC) Web site . Also available in French from the SOGC Web site .

Print copies: Available from the Society of Obstetricians and Gynaecologists of Canada, La société des obstétriciens et gynécologues du Canada (SOGC) 780 promenade Echo Drive Ottawa, ON K1S 5R7 (Canada); Phone: 1-800-561-2416.

Availability of Companion Documents

None available

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on April 11, 2012. The information was verified by the guideline developer on May 10, 2012.

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